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Abnormal Endothelium-Dependent Coronary Vasomotion in Hypertensive Patients

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Coronary vasomotion is abnormal in hypertensive patients, as evidenced by reduced coronary vasodilator reserve, but endothelium-dependent coronary vasomotion in hypertensive patients has not been studied. To assess the integrity of endothelium-dependent vasodilation, the response of coronary arteries to acetylcholine (an endothelium-dependent vasodilator) and nitroglycerin (an endothelium-independent vasodilator) was studied in 14 patients undergoing cardiac catheterization. Eight patients with essential hypertension were compared with six normotensive patients. None had obstructive disease detectable by coronary arteriography. Coronary artery diameter was measured with digital-subtracted arteriography and coronary blood flow velocity with a Doppler flow velocity catheter.

At baseline, coronary artery diameter was similar in the hypertensive and the normotensive control patients (2.4 ± 0.3 vs. 2.8 ± 0.7 mm). During intracoronary acetylcholine infusion (30 μg/min), coronary artery diameter decreased to 1.3 ± 0.7 mm in the hypertensive patients ($p < 0.005$), but was unchanged (2.7 ± 0.8 mm) in the normotensive patients. With intracoronary nitroglycerin (200 μg), coronary artery diameter increased significantly in both groups. Calculated coronary blood flow decreased during acetylcholine infusion by 59 ± 31% in the hypertensive patients but increased by 3 ± 3% in the normotensive group ($p < 0.005$). There was a significant negative correlation between the percent change in estimated coronary blood flow during acetylcholine infusion and mean arterial pressure measured at baseline ($r = 0.67$, $p < 0.02$).

Therefore, these hypertensive patients exhibited marked coronary vasoconstriction in response to intracoronary acetylcholine but normal vasodilation in response to nitroglycerin, suggesting abnormal endothelium-dependent vasodilation. The latter may be a mechanism contributing to reduced coronary vasodilator reserve and angina pectoris in hypertensive patients.

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Angina pectoris is frequently reported by hypertensive patients. Although angina is often due to atherosclerotic epicardial vessel narrowing, it can also occur in hypertensive patients in the absence of epicardial coronary artery disease (1–4). Previous studies (1,2,4) have shown that hypertensive patients with angina can have a reduction in maximal coronary vasodilation in response to pharmacologic vasodilation or pacing-induced stress. A recent study (4) indicated that myocardial ischemia and reduced coronary vasodilation can occur in hypertensive patients who have neither atherosclerotic coronary disease nor left ventricular hypertrophy. Therefore, extrinsic compression of the coronary microvasculature by hypertrophied myocardium does not appear to be the only mechanism of reduced coronary vasodilation in hypertensive patients. That recent study (4) suggested that an intrinsic abnormality of the coronary vasculature may limit coronary vasodilation in these patients.

One potential mechanism to explain reduced coronary vasodilation in hypertensive patients is an abnormality of endothelium-dependent vasodilation. In 1980, Furchgott and Zawadzki (5) first observed that the endothelium modulates arterial tone by releasing an endothelium-derived relaxing factor. Many studies (6–8) have now demonstrated that the endothelium releases several relaxing and constricting factors in response to a variety of stimuli and that endothelial-dependent vasomotion can be impaired in many diseases including hypertension.

Studies in hypertensive animal models (9–13) have shown that endothelium-dependent vasodilation is impaired in both large and small arteries. Several studies (10,14) have demonstrated the presence of endothelium-derived constricting factors in spontaneously hypertensive rats. In addition, it has been shown (15) that decreased endothelium-dependent vasodilation can be partially reversed in rats with salt-induced hypertension when the hypertension is normalized. These previous animal studies (9–15) have provided strong evidence that endothelium-dependent vasomotion is abnormal in hypertensive animals.

Human studies (16–19) have demonstrated abnormal coronary artery endothelial function in patients with atherosclerosis and several other diseases. In one previous study, the investigators (16) demonstrated paradoxic coronary vaso-

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constriction in response to acetylcholine (which is normally an endothelium-dependent vasodilator) in patients with atherosclerotic coronary artery disease. The same group (20) also reported that risk factors for atherosclerotic coronary artery disease are associated with abnormal coronary vasomotion in patients with early atherosclerotic disease. However, in these patients with early atherosclerosis hypertension did not appear to be an independent predictor of coronary vasoconstriction.

Endothelium-dependent coronary vasodilation has not been studied previously in hypertensive patients, although two studies (21,22) have examined endothelium-dependent vasomotion in the peripheral vasculature of such patients. In both studies (21,22), forearm blood flow increased to a lesser degree in response to acetylcholine in hypertensive patients than in normotensive control subjects, indicating endothelial impairment of the peripheral vasculature in hypertensive patients.

On the basis of studies of endothelium-dependent vasomotion in animal models of hypertension and the previous clinical studies, we hypothesized that there is an abnormality of endothelium-dependent coronary vasomotion in hypertensive patients. To study this hypothesis, we examined the coronary vasomotor response to the endothelium-dependent vasodilator acetylcholine and the endothelium-independent vasodilator nitroglycerin in patients undergoing diagnostic cardiac catheterization for the evaluation of chest pain.

Methods

Patient selection. Fourteen patients with a history of angina-like chest pain undergoing diagnostic cardiac catheterization were studied. Eight patients, two women and six men, with a mean age of 52 ± 9 years, had a history of essential hypertension requiring long-term therapy. Six patients, five women and one man with a mean age of 52 ± 14 years, had no history of hypertension and were normotensive during the hospital stay. Cardioactive medications were withheld in all patients for >24 h before catheterization. The catheterization protocol was approved by the Institutional Review Board of University Hospital and all patients gave informed consent before undergoing the procedure.

In all patients, normal coronary artery anatomy was documented by coronary arteriography and normal left ventricular function by contrast ventriculography. A period of 15 min was allowed between the injection of contrast medium and initiation of the experimental protocol.

Catheter placement. A bipolar pacing catheter was introduced and advanced to the pulmonary artery to be used for right ventricular pacing if necessary during the study protocol. A standard 8F coronary angioplasty guiding catheter was placed at the left coronary artery ostium. A 3F Doppler flow velocity catheter (23) (Millar Instruments) was introduced into the left anterior descending or left circumflex artery over a 0.014 in. (0.036 cm) floppy guide wire. The flow velocity catheter was advanced approximately 1 to 2 cm into the study artery (the left anterior descending artery in 13 patients and the left circumflex artery in 1 patient). The guide wire was removed from the flow velocity catheter and the central lumen was used for subselective drug infusion into the coronary artery. The Doppler range control was adjusted to give maximal peak blood flow velocity at baseline and the range control was not changed thereafter. Constant catheter position was maintained by repeatedly checking the position with fluoroscopy. During flow velocity measurements, the guiding catheter was retracted slightly from the left coronary ostium to allow unimpeded blood flow into the left coronary artery. Phasic Doppler flow velocity was recorded and peak diastolic flow velocity data are reported. The guiding catheter was used to monitor systemic arterial blood pressure and mean arterial pressure was determined electronically.

Study protocol. At baseline, mean arterial pressure and coronary flow velocity were recorded. Coronary arteriography was performed with use of both cinearteriography and digital subtraction arteriography. Acetylcholine chloride (Sigma Chemicals) was infused subselectively into the study artery through the flow velocity catheter at a rate of 15 μg/min (0.5 ml/min). If a left anterior descending or circumflex artery blood flow of 80 ml/min is assumed, this infusion rate resulted in an intracoronary concentration of approximately 10^{-6} *M*. Acetylcholine was infused for 3 min and repeat recordings of mean arterial pressure and coronary flow velocity were obtained. Coronary arteriography was repeated.

When hemodynamic variables returned to baseline values, acetylcholine infusion was restarted at 30 μg/min (1 ml/min). The infusion was continued for 3 min and mean arterial pressure and coronary flow velocity were again recorded and coronary arteriography was repeated.

Next, nitroglycerin (200 μg) (Dupont Critical Care) was administered as a single bolus injection through the left coronary artery guiding catheter (24). Nitroglycerin was administered into the left main coronary artery rather than subselectively into the study artery because of ease of rapid administration and because the effect of selective and subselective administration is similar as a result of systemic recirculation of nitroglycerin. Approximately 30 s after nitroglycerin administration, mean arterial pressure and coronary flow velocity were recorded and coronary arteriography was repeated.

Coronary arteriography. Coronary arteriography was performed in orthogonal right anterior oblique and left anterior oblique views that best showed the study artery without overlap with other vessels. Camera angulation and the height of the image intensifiers were maintained constant during all subsequent arteriograms. Coronary arteriograms were obtained by injecting nonionic contrast medium (Iopamidol, Squibb Diagnostics).

Coronary arteriograms were recorded with use of an ADAC Laboratories 4100 Digital Radiography System interfaced with a Philips X-ray unit. Exposure variables were controlled automatically and digital images were recorded

with use of a 6-in. (15-cm) image intensifier and stored in a 512 × 512 pixel matrix. Vessel diameter was measured with an automated system that uses an edge-detection algorithm and averages the vessel diameter along a defined length of vessel (25). Absolute vessel diameter was calculated by comparing vessel diameter with the known diameter of the arteriographic catheter. The accuracy of this system has been validated extensively and vessel diameters measured with this system have shown excellent correlation with the known lumens of drilled plastic implants or with pressure-fixed coronary arteries measured histologically (25–27). The reproducibility of this system was validated in our laboratory in 20 patients undergoing successive arteriography 5 min apart and the measured vessel diameters showed agreement within 1% ($r = 0.95$, SEE = 0.19).

An end-diastolic frame was chosen from the digital subtraction arteriogram for analysis. A segment of the study artery that was relatively straight and free of side branches and that was approximately 1 to 2 cm distal to the tip of the infusion catheter was chosen for measurement of vessel diameter. In one patient, the digital-subtracted image was unavailable and the vessel diameter was measured from a projected cine image with electronic calipers (Brown and Sharpe Manufacturing).

To ensure that differences in diameter of the study artery were not due to variability in contrast injection technique, the coronary artery that was not receiving the drug infusion was also measured at baseline and during each drug infusion. For example, in patients in whom acetylcholine was infused into the left anterior descending coronary artery, the diameter of both this artery and the left circumflex artery was measured—the former to measure the drug effects and the latter to ensure that there was no variability in contrast injection technique.

Coronary flow velocity and velocity area index. To estimate volumetric coronary blood flow, a velocity-area index (VAI) was calculated as follows: VAI = coronary flow velocity × $\pi(D/2)^2$, where coronary flow velocity is the peak Doppler flow velocity and D is the cross-sectional coronary artery diameter (17).

Statistical analysis. Data are presented as mean values ± SD in the text and mean values ± SEM in the figures. Hypertensive subjects were compared with normotensive subjects with use of a nonpaired *t* test for continuous variables. Measurements during drug infusions were compared with baseline measurements with use of paired *t* tests. A p value ≤0.05 defined statistical significance.

Results

Patient characteristics. Six of the eight hypertensive patients described their chest pain as a "tightness" or "heaviness" and two described it as "sharp" or "aching." In these patients, long-term medical therapy consisted of a calcium channel blocking agent in seven, a beta-adrenergic blocking agent in three, a diuretic drug in three, a long-acting nitrate in five, an angiotensin-converting enzyme inhibitor in two and aspirin in one. Two patients had a decrease in the frequency of chest pain after starting beta-blocking therapy for hypertension and one patient had relief of chest pain with a nitrate. Five patients had previous hospital admissions for suspected myocardial infarction and one of these had a previously documented non-Q wave myocardial infarction. All eight hypertensive patients underwent exercise tolerance testing; the test results were interpreted as equivocal in five and as normal in three.

Four of the six normotensive patients described their chest pain as "pressure" or "heaviness" and two as "sharp" or "aching." In these patients, long-term medical therapy consisted of a calcium channel blocking agent in four, a beta-adrenergic blocking agent in two, a long-acting nitrate in one and aspirin in one. Two normotensive patients had relief of chest pain with a nitrate; four had previous hospital admissions for suspected myocardial infarction but none had a previous documented infarction. In three normotensive patients results of exercise tolerance testing were interpreted as equivocal and in one normotensive patient they were interpreted as normal.

All study patients had all cardioactive medications withheld for >24 h before cardiac catheterization. Aspirin was taken by one hypertensive patient 2 days before the study and by one normotensive patient 3 days before the study.

The two groups were similar with respect to serum cholesterol levels (225 ± 40 mg/dl in the hypertensive patients and 234 ± 57 mg/dl in the normotensive patients) and the frequency of other comorbid illness.

Baseline hemodynamics. The baseline mean arterial pressure was 119 ± 23 mm Hg in the hypertensive patients compared with 85 ± 10 mm Hg in the normotensive patients ($p < 0.01$). Heart rate was similar in the hypertensive and normotensive patients (87 ± 16 vs. 83 ± 15 beats/min). The two groups had a similar baseline coronary diameter (hypertensive 2.4 ± 0.3 mm, normotensive 2.6 ± 0.7 mm). At baseline, coronary flow velocity was not significantly different between groups (hypertensive 8.1 ± 7.4, normotensive 5.7 ± 1.9 cm/s). Velocity-area index was also not significantly different between the two groups (hypertensive 32.5 ± 27.5 vs. normotensive 37.2 ± 20).

Hemodynamic and vessel diameter changes during acetylcholine infusion. In the hypertensive patients, there was a progressive decrease in vessel diameter during acetylcholine infusions (Fig. 1). The vessel diameter decreased from 2.4 ± 0.3 mm at baseline to 1.5 ± 0.8 during the 15-μg/min infusion ($p < 0.05$) and to 1.3 ± 0.7 during the 30-μg/min infusion ($p < 0.005$ compared with baseline). The decrease in vessel diameter was visually obvious on arteriography (Fig. 2) and in one patient, the left anterior descending artery became totally occluded during acetylcholine infusion, requiring immediate treatment with intracoronary nitroglycerin. Four of the hypertensive patients with coronary vasoconstriction during acetylcholine infusion reported having substernal chest pain during the infusion.

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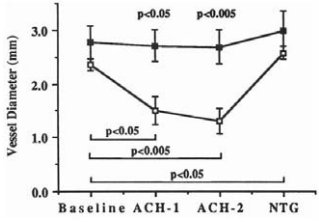


Figure 1. Coronary artery diameter in eight hypertensive patients (**open squares**) and six normotensive control patients (**closed squares**) during intracoronary acetylcholine infusion of 15 μg/min (ACH-1) and 30 μg/min (ACH-2) and nitroglycerin infusion of 200 μg (NTG). **Error bars** in this and subsequent figures represent standard error of the mean.

During the maximal acetylcholine infusion, mean arterial pressure was unchanged in the hypertensive patients (124 ± 22 mm Hg). Heart rate also remained unchanged (88 ± 16 beats/min). Coronary flow velocity was 8.2 ± 11 cm/s (not significantly changed from baseline). Velocity-area index decreased from 32.5 ± 27.5 at baseline to 18.1 ± 26.3 during peak acetylcholine infusion ($p < 0.02$).

Normotensive patients. In marked contrast to the hypertensive patients, the normotensive patients did not show a significant decrease in coronary vessel diameter during acetylcholine infusion (Fig. 1). Coronary diameter in this group was 2.8 ± 0.7 at baseline and 2.7 ± 0.7 mm during the 15-μg/min infusion ($p < 0.02$ vs. 1.5 ± 0.8 mm in the hypertensive patients) and 2.7 ± 0.8 during the 30-μg/min infusion ($p < 0.005$ vs. 1.3 ± 0.7 mm in the hypertensive patients). The average decrease in coronary vessel diameter during acetylcholine infusion in the normotensive patients was 3 ± 5%, which was significantly less than the average decrease of 44 ± 26% observed in the hypertensive patients ($p < 0.005$).

During the maximal acetylcholine infusion, mean arterial pressure was unchanged in the normotensive patients (87 ± 10 mm Hg). Heart rate and coronary flow velocity were not significantly changed during acetylcholine infusion (77 ± 17 beats/min and 6.3 ± 3 cm/s, respectively). Velocity-area index was 37.2 ± 20 at baseline and was not significantly changed during acetylcholine infusion (39.7 ± 29.8). At baseline, velocity-area index in the normotensive patients was not significantly different from that in the hypertensive patients. During maximal acetylcholine infusion, velocity-area index increased by 3 ± 3% in the normotensive patients compared with a 59 ± 31% decrease in the hypertensive patients ($p < 0.005$) (Fig. 3). Among the hypertensive and normotensive patients, there was a negative correlation between mean arterial pressure measured at baseline and the percent change in velocity-area index during acetylcholine infusion ($r = 0.67$, $p < 0.05$) (Fig. 4).

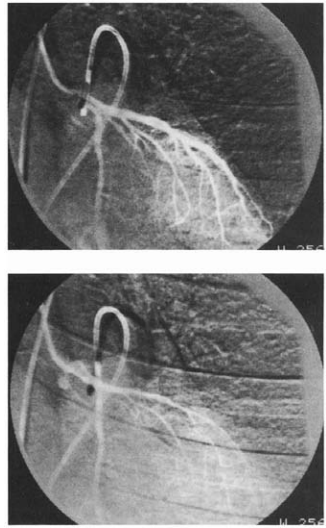


Figure 2. Digital-subtracted arteriogram of the left coronary artery in the right anterior oblique view during baseline conditions (**top**) and during acetylcholine infusion (30 μg/min) (**bottom**), showing marked diffuse spasm of the left anterior descending coronary artery in response to the infusion.

To ensure that the observed changes in coronary artery diameter were not due to differences in contrast injection technique, the diameter of the noninfused coronary artery was also measured. In the hypertensive patients, the noninfused artery measured 2.6 ± 0.7 mm at baseline and was unchanged during acetylcholine infusion (2.5 ± 0.6 and 2.5 ± 0.6 mm during the two infusions). Similarly, in the normotensive patients, the noninfused coronary artery measured 2.7 ± 0.6 at baseline and was unchanged during acetylcholine infusion (2.7 ± 0.6 mm and 2.7 ± 0.6 mm during the two infusions).

Hemodynamic and vessel diameter changes during nitroglycerin injection. In the hypertensive patients, the vessel diameter increased normally after nitroglycerin injection, from 2.4 ± 0.3 to 2.6 ± 0.4 mm ($p < 0.05$) (Fig. 1). Coronary flow velocity was unchanged (13.1 ± 18.8 cm/s), as was velocity-area index (60.4 ± 76.1). Mean arterial pressure and heart rate were not significantly changed (115 ± 27 mm Hg and 82 ± 13 beats/min, respectively).

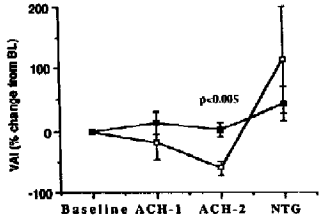


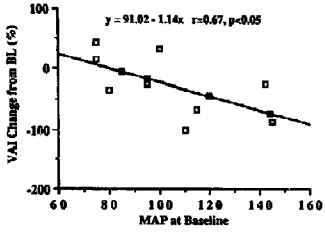
Figure 3. Percent change from baseline (BL) in volume-area index (VAI) in eight hypertensive patients (open squares) and six normotensive control patients (closed squares) during acetylcholine infusion of 15 μg/min (ACH-1) and 30 μg/min (ACH-2) and nitroglycerin infusion of 200 μg (NTG).

In the normotensive patients, the coronary vessel diameter also increased after nitroglycerin injection, from 2.8 ± 0.7 to 3 ± 0.8 mm ($p = 0.08$) (Fig. 1). This 10 ± 8% increase in coronary vessel diameter after nitroglycerin injection in the normotensive subjects was similar to the 12 ± 9% increase in the hypertensive patients. In the normotensive group there was no significant change in coronary flow velocity (6.3 ± 1.3 cm/s) or velocity-area index (49.2 ± 34). Mean arterial pressure decreased from 85 ± 11 to 80 ± 12 mm Hg ($p < 0.05$). Heart rate was unchanged (87 ± 17 beats/min).

Discussion

Coronary artery responses to acetylcholine. The findings in this study indicate that hypertensive patients have a markedly abnormal coronary vasoconstrictor response to intracoronary acetylcholine compared with that of normotensive subjects. During acetylcholine infusion, the hypertensive patients had a mean reduction in coronary artery diameter of 44% compared with a reduction of only 3% in the normotensive patients. Because acetylcholine normally acts as an endothelium-dependent vasodilator, these data indicate that the functional integrity of the coronary endothelium is impaired in these hypertensive patients.

Figure 4. Relation between the percent change from baseline (BL) in volume-area index (VAI) during acetylcholine infusion (30 μg/min) and mean arterial pressure (MAP) at baseline in the 13 study patients.



Coronary blood flow velocity was unchanged in both the hypertensive and the normotensive patients during acetylcholine infusion. However, there was a 59% decrease in the calculated velocity-area index in the hypertensive patients during acetylcholine infusion compared with a 3% increase in the normotensive patients, suggesting a decrease in volumetric coronary blood flow in the hypertensive patients during acetylcholine infusion. There was a significant negative correlation between the change in coronary blood flow during acetylcholine infusion and the baseline mean arterial pressure, suggesting that the observed abnormality in endothelium-dependent vasomotion was more severe in patients with more severe hypertension. Given the marked epicardial coronary artery vasoconstriction that was observed, it is not possible to discern whether the apparent decrease in coronary blood flow was due to increased coronary resistance at the epicardial or the microvascular level.

Coronary artery responses to nitroglycerin. The hypertensive and normotensive patients were similar with respect to the change in coronary artery diameter after nitroglycerin injection; both groups showed vasodilation. Because nitroglycerin is an endothelium-independent vasodilator, these data indicate that the coronary arteries of the hypertensive patients are capable of dilating to a degree similar to that observed in the arteries of normotensive patients. The normal response to nitroglycerin in the hypertensive patients indicates that the defect in coronary vasodilation in response to acetylcholine in these patients is not due to hyporesponsiveness of the vascular smooth muscle to endothelium-derived relaxing factor because this factor has been shown to be a nitrovasodilator and would be expected to have the same effect as nitroglycerin (28). The degree of coronary artery vasodilation that was seen in response to nitroglycerin in the hypertensive and normotensive patients is similar to that previously reported (24).

The differences between the hypertensive and normotensive subjects were not due to differences in age or serum cholesterol because these variables were similar in the two groups. Furthermore, the reduction in coronary artery diameter in the hypertensive patients during acetylcholine infusion could not be due to differences in contrast injection technique. Simultaneous contrast injection into the coronary artery branch not receiving acetylcholine (the circumflex artery in most patients) showed that the artery not receiving acetylcholine was unchanged in diameter from baseline in both groups, indicating consistent contrast injection throughout the study.

Comparison with previous studies. The lack of coronary vasodilation with acetylcholine observed in the normoten-

sive patients in this study is in contrast to results of a previous study (16) that described vasodilation, but is in agreement with data from three previous studies (17–19) that reported a lack of vasodilation with acetylcholine in patients with arteriographically normal coronary arteries. The difference between our study and the previous study by Ludmer et al. (16) may be related to differences in study protocols. In our study, we infused acetylcholine subselectively into the coronary artery through an infusion catheter to eliminate spillage from the study artery, resulting in higher doses of acetylcholine in that artery. A previous study (29) showed that acetylcholine in higher doses causes mild vasoconstriction of arteriographically normal coronary arteries, as was seen in our control patients and in those of previous studies (17–19). Nevertheless, at the concentrations of acetylcholine used in this study, there was a marked difference in the coronary vasomotor response to acetylcholine between the hypertensive and normotensive patients.

A previous study (30) demonstrated that endothelium-dependent coronary vasodilation is impaired in patients with evidence of early atherosclerosis. That study (30) classified patients according to whether there were intraluminal irregularities on coronary arteriography suggestive of early atherosclerosis and found that patients with such a finding had vasoconstriction in response to acetylcholine. The hypertensive patients in our study had no intraluminal irregularities or other arteriographic evidence of early atherosclerosis, making early atherosclerosis an unlikely explanation for the observed abnormal coronary vasomotion. It is known that coronary arteriography underestimates the degree of atherosclerosis (31). Because hypertension is a known risk factor for the development of atherosclerosis, it is possible that arteriographically undetectable atherosclerosis accounts for the observed abnormality in endothelium-dependent vasomotion. However, patients with more severe hypertension at baseline study had more severe vasoconstriction, as evidenced by the negative correlation between the baseline blood pressure and the change in velocity-area index during acetylcholine infusion. This finding suggests that the abnormal vasoconstrictive response to acetylcholine was due to the hypertension and not to early undetectable atherosclerosis. Nevertheless, it is not possible to discern whether the abnormal vasoconstriction was due to acute hypertension or to vascular changes associated with chronic hypertension.

Potential mechanisms. Acetylcholine-induced vasoconstriction in the hypertensive patients may be due to a relative decrease in release of endothelium-derived relaxing factor or possibly an increase in the release of an endothelium-dependent vasoconstricting substance (32,33). Luscher et al. (33) demonstrated that acetylcholine induces vasoconstriction in the spontaneously hypertensive rat. The vasoconstriction can be inhibited with indomethacin, an inhibitor of cyclooxygenase, indicating that the constricting factor is a metabolite of arachidonic acid. It is possible that the coronary constriction we observed was due to either increased release of or increased sensitivity to an endothelium-derived constricting factor. Whether acetylcholine-induced coronary vasoconstriction in hypertensive patients can be reversed by inhibiting arachidonic acid metabolism with drugs such as indomethacin is a question requiring further study.

Only four of the eight hypertensive patients and none of the six normotensive patients experienced reproducible angina during acetylcholine infusion. Most likely, coronary constriction induced by acetylcholine in this protocol was not prolonged enough to uniformly cause myocardial ischemia under these conditions. It was not our purpose to reproduce clinical symptoms in these patients, but rather to study coronary physiology in hypertensive patients. However, it is interesting to speculate how this abnormality of endothelial-dependent vasomotion might contribute to angina in such patients. It is known that endothelium-derived relaxing factor has a role in coordinating relative myocardial perfusion (34) and may cause a preferential increase in subendocardial perfusion (35). An abnormality in endothelium-dependent vasodilation may therefore have important adverse effects on microvascular blood flow in hypertensive patients. Previous studies (1–4) have shown that hypertensive patients have decreased coronary vasodilator reserve and it is possible that this is at least partially caused by regional hypoperfusion that results from impaired endothelium-dependent vasodilating mechanisms.

Conclusions. Hypertensive patients have markedly abnormal coronary vasoconstriction in response to intracoronary infusion of acetylcholine, an endothelium-dependent vasodilator, but have a normal response to intracoronary nitroglycerin, an endothelium-independent vasodilator. These findings suggest that endothelium-dependent coronary vasodilation is abnormal in these hypertensive patients and have important implications concerning the pathophysiology of the cardiac manifestations of hypertension.

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